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Cross-sections for (*p*,*x*) reactions on natural chromium for the production of ^{52,52m,54}Mn radioisotopes

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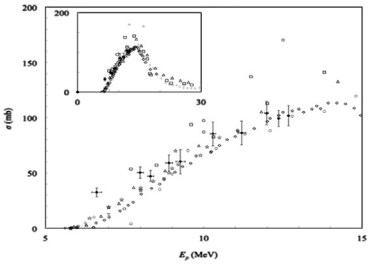
HIGHLIGHTS

- Produced large batch of natural Cr foils for cyclotron bombardment.
- Bombarded stacked foil targets with protons < 14 MeV to measure cross-sections.
- Report new cross-section results for the ^{nat}Cr(*p*,*x*)^{52}Mn, ^{nat}Cr(*p*,*x*)^{52m}Mn, and ^{nat}Cr(*p*,*x*)^{54}Mn reactions.

GRAPHICAL ABSTRACT

The production of positron-emitting isotopes of manganese is potentially important for developing contrast agents for dual-modality positron emission tomography and magnetic resonance (PET/MR) imaging, as well as for *in vivo* imaging of the biodistribution and toxicity of manganese. The decay properties of ^{52}Mn make it an excellent candidate for these applications, and it can easily be produced by bombardment of a chromium target with protons or deuterons from a low-energy biomedical cyclotron. Several parameters that are essential to this mode of production—target thickness, beam energy, beam current, and bombardment time—depend heavily on the availability of reliable, reproducible cross-section data. This work contributes to the routine production of ^{52g}Mn for biomedical research by contributing experimental cross-sections for natural chromium (^{nat}Cr) targets for the ^{nat}Cr(*p*,*x*)^{52g}Mn reaction, as well as for the production of the radiocontaminants ^{52m,54}Mn.



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ABSTRACT

The production of positron-emitting isotopes of manganese is potentially important for developing contrast agents for dual-modality positron emission tomography and magnetic resonance (PET/MR) imaging, as well as for *in vivo* imaging of the biodistribution and toxicity of manganese. The decay properties of ^{52}Mn make it an excellent candidate for these applications, and it can easily be produced by bombardment of a chromium target with protons or deuterons from a low-energy biomedical cyclotron. Several parameters that are essential to this mode of production—target thickness, beam energy, beam current, and bombardment time—depend heavily on the availability of reliable, reproducible cross-section data. This work contributes to the routine production of ^{52g}Mn for biomedical research by

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^{54}Mn
Cross-section
Solid target
Radiometal
PET isotopes
Isotope production

contributing experimental cross-sections for natural chromium (^{nat}Cr) targets for the ^{nat}Cr(p,x)^{52g}Mn reaction, as well as for the production of the radiocontaminants ^{52m,54}Mn.

1. Introduction

Both historically and in recent years, there has been significant interest in the biomedical roles and applications of manganese. A search of the PubMed database in 2013 showed that the number of publications with manganese in the title had an average annual increase of 7% or more over the previous five, ten, twenty, and fifty years, with an average approaching 800 publications per year over the five previous years (PubMed, 2013). This growing interest likely comes from several characteristics of manganese that have important consequences for biology and medicine, including: its roles as an essential nutrient in mammals; its toxicity in large amounts; its role in plant photosynthesis; and its paramagnetism in the Mn^{2+} oxidation state. Thus, there are many potential interesting applications for a manganese radiotracer, particularly for an isotope that is imageable by positron emission tomography (PET), which has very high sensitivity and better spatial resolution than other nuclear imaging modalities. Imageable isotope(s) of manganese could facilitate *in vivo* studies that utilize manganese as a radiotracer for antibodies, nanoparticles, etc. or as a means to image the biodistribution of manganese cations.

Based on nuclear decay properties, ^{52}Mn is a good candidate for these applications. This isotope has a half-life ($t_{1/2}$=5.6 d) that would make it convenient for processing, labeling, and shipping, as well as for imaging studies that require time points that are several days post-injection. ^{52}Mn emits positrons with a branching ratio ($I_{\beta+}$=29.6%) (Huo et al., 2007) that is comparable to other PET radiometals (e.g., ^{64}Cu and ^{89}Zr) and with a very low average positron energy ($E_{\beta+}$=242 keV) (Huo et al., 2007) that is even lower than ^{18}F and therefore gives even better spatial resolution in PET (Prince and Links, 2005). However, ^{52}Mn also emits significant gamma radiation (Smith and Stabin, 2012), which can increase dose to research personnel and laboratory animals, as well as cause artifacts in PET. ^{52m}Mn has also been investigated in PET studies as it has a high branching ratio for positron emission ($I_{\beta+}$=95.0%), but its utility is limited by a short half-life ($t_{1/2}$=21.1 min), very high average positron energy ($E_{\beta+,avg}$=1170 keV), and significant gamma radiation emission (Huo et al., 2007). Despite the interest in imaging ^{52}Mn and ^{52m}Mn, routine production of useful quantities of these isotopes with high purity is still being developed (Buchholz et al., 2013; Topping et al., 2013).

Essential to any routine isotope production protocol is the ability to select target thickness, beam energy, beam current, and bombardment time based on predicted yield, which in turn is based on nuclear cross-section data. Target thickness and beam energy are typically selected so that the entry and exit energies of the beam will span a region of the excitation function with high cross-sections for the product and little or no cross-sections for other, competing reaction channels that may produce contaminant isotopes. Designing production runs to optimize this energy "window" can improve yield and radionuclidic purity of the final product. Thus, it is important to have accurate cross-section data for not only the reactions that produce the desired product, but also for the reactions that would produce contaminant isotopes. In this investigation, we bombarded natural chromium targets (^{nat}Cr=^{50}Cr (4.3%), ^{52}Cr (83.8%), ^{53}Cr (9.5%), ^{54}Cr (2.4%)), which could potentially produce several product isotopes. This work focused primarily on measurements for the production of ^{52}Mn, but also for ^{52m}Mn and ^{54}Mn as radiocontaminants. Only a few data sets are currently available with points at proton beam energy (E_p) ≤ 14 MeV for the ^{nat}Cr(p,x) reactions that produce ^{52,52m}Mn (Barrandon et al., 1975; Buchholz et al., 2013; West Jr et al., 1987), and there are only data sets from enriched targets available for ^{54}Mn at these low energies (Gusev et al., 1990; Johnson et al., 1960; Kailas et al., 1975; Levkovskij, 1991; Skakun et al., 1986; Zyskind et al., 1978). In this work, we contribute new experimental cross-section data for each of these (p,x) reactions that produce ^{52,52m,54}Mn from bombardment of natural chromium with protons at low-energies.

2. Methods

2.1. Target preparation

2.1.1. Materials

Nitric acid (70%) was purchased from Sigma-Aldrich (St. Louis, MO, USA). Copper sheet (0.762 mm thick, 99.9% purity) was purchased from ESPI Metals (Ashland, OR, USA), and copper foil (0.025 mm, 99.999% purity) was purchased from Alfa Aesar (Ward Hill, MA, USA). Natural abundance chromium was electroplated by Four Star Finishing (St. Louis, MO, USA).

2.1.2. Production of thin ^{nat}Cr foils

Copper monitor foils were produced by punching ~9.5 mm disks from 0.762 mm (nominal) copper foil. However, Cr metal is very brittle, so cutting or punching disks from thin Cr foil was not feasible. Furthermore, thin Cr foil was not commercially available without a permanently attached Mylar (polyethylene terephthalate) backing.

Therefore, we developed a method for fabricating batches of thin Cr foils that would fit into target holders for one of the solid target stations connected to our cyclotron—without cutting Cr metal. Thin, circular foil disks were produced through a process of electrodeposition of non-enriched Cr onto small plugs of Cu backing material, followed by removal of the Cu backing, similar to a method previously used by Tanaka and Furukawa (1959). Holes (~10 mm diameter) were cut or punched from Cu sheet, and these holes were then filled using ~9.8 mm Cu disks that were punched from elsewhere on the Cu sheet. On the "back" side of the plate, these disks were fixed in place by soldering the back of each disk to one of several long strips of thick (~1–2 mm diameter) bus bar wire that was also soldered to the large copper plate. Fig. S1 shows a sample that contained a 13 × 13 grid of copper plugs soldered in place on the back.

The back of the sample was masked with a vinyl lacquer, and the entire sample was submerged (while connected to the cathode) into an industrial-scale chrome plating bath, and the unmasked side of the sample was electroplated with Cr. This bath electroplated with "hard chrome," meaning thick (tens to hundreds of μm), ultra hard deposits of pure Cr metal. (The more popular type of chrome plating, "decorative chrome", is roughly 1000 × thinner and usually plated over nickel or copper). The bath was an aqueous solution of 100:1 chromic acid (H_2CrO_4) and sulfuric acid (H_2SO_4). (Safety note: The chromic acid was made from chromium(VI) oxide (CrO_3 powder), which is acutely toxic (oral, inhaled, or dermal), damaging to eyes and skin, and carcinogenic,